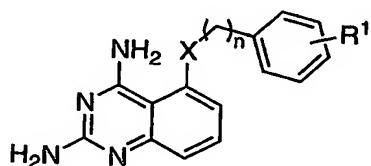


-37 -

WE CLAIM:

1. A method of treating conditions that benefit from an inhibition of dihydrofolate reductase (DHFR), comprising administering to an animal in need thereof, an effective amount of compound selected from one or more of a compound of Formula I, and pharmaceutically acceptable salts and solvates thereof:

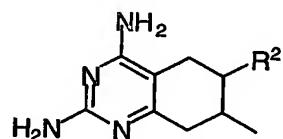


wherein

10 R¹ is selected from the group consisting of C₁₋₄alkyl, halo and CF₃;
 X is O or S; and
 n is 0 or 1.

2. The method according to claim 1, wherein the compound of Formula I is selected from one or more of compound 1, 2, 3, 4 and 5 as shown in Table 1, and pharmaceutically acceptable salts and solvates thereof.

3. A method of treating conditions that benefit from an inhibition of dihydrofolate reductase (DHFR), comprising administering to an animal in need thereof, an effective amount of compound selected from one or more of a compound of Formula II, and pharmaceutically acceptable salts and solvates thereof:



wherein R² is selected from the group consisting of H and C₁₋₄alkyl.

-38 -

4. The method according to claim 13, wherein the compound of Formula II is selected from the group consisting of compound 6 and 7 as shown in Table 1, or pharmaceutically acceptable salts, solvates or hydrates thereof.
5. 5. A method of treating conditions that benefit from an inhibition of DHFR, comprising administering to an animal in need thereof, an effective amount a compound selected from one or more of compounds 8 to 11 as shown in Table 1 and pharmaceutically acceptable salts and solvates thereof.
- 10 6. A method of treating bacterial infections comprising administering an effective amount of a compound selected from one or more of:
 - (a) a compound of Formula I, as defined in claim 1 or 2;
 - (b) a compound of Formula II, as defined in claim 3 or 4;
 - (c) compounds 8-11 as shown in Table 1; and
 - (d) pharmaceutically acceptable salts and solvates of (a), (b) and (c), to a cell or animal in need thereof.
- 15 7. A use of a compound of Formula I as defined in claim 1 or 2 to treat conditions that benefit from an inhibition of DHFR.
- 20 8. A use of a compound of Formula I as defined claim 1 or 2 to prepare a medicament conditions that benefit from an inhibition of DHFR.
- 25 9. A use of a compound of Formula II as defined in claim 3 or 4 to treat conditions that benefit from an inhibition of DHFR.
10. A use of a compound of Formula II as defined in claim 3 or 4 to prepare a medicament to treat conditions that benefit from an inhibition of DHFR.
- 30 11. A use of a compound selected from one or more of compounds 8 to 11 as shown in Table 1 to treat conditions that benefit from an inhibition of DHFR.

12. A use of a compound selected from one or more of compounds 8 to 11 as shown in Table 1 to prepare a medicament to treat conditions that benefit from an inhibition of DHFR.

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13. A use of a compound selected from one or more of:

- (a) a compound of Formula I, as defined in claim 1 or 2;
- (b) a compound of Formula II, as defined in claim 3 or 4;
- (c) compounds 8-11 as shown in Table 1; and

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(d) pharmaceutically acceptable salts and solvates of (a), (b) and (c), to treat bacterial infections.

14. A use of a compound selected from one or more of:

- (a) a compound of Formula I, as defined in claim 1 or 2;
- (b) a compound of Formula II, as defined in claim 3 or 4;
- (c) compounds 8-11 as shown in Table 1; and
- (d) pharmaceutically acceptable salts and solvates of (a), (b) and (c),

to prepare a medicament or pharmaceutical composition to treat bacterial infections in a cell or animal in need thereof.

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15. The method according to claim 6, wherein the bacterial infection is selected from an *E. coli*, *Bacillus Subtilis*, *Streptococci*, *Staphylococci*, *Enterococci*, *Salmonella*, *Haemophilus influenza*, *Pseudomonas aeruginosa*, *Bacillus anthracis* and *Helicobacter pylori* infection.

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16. The use according to any one of claims 13-14, wherein the bacterial infection is selected from an *E. coli*, *Bacillus Subtilis*, *Streptococci*, *Staphylococci*, *Enterococci*, *Salmonella*, *Haemophilus influenza*, *Pseudomonas aeruginosa*, *Bacillus anthracis* and *Helicobacter pylori* infection.

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-40 -

17. The method according to claim 5, wherein the compound is compound 9 as shown in Table 1 and pharmaceutically acceptable salts and solvates thereof.
- 5 18. The method according to claim 7, wherein the compound is compound 9 as shown in Table 1 and pharmaceutically acceptable salts and solvates thereof.
- 10 19. The use according to any one of claims 11-14 wherein the compound is compound 9 as shown in Table 1 and pharmaceutically acceptable salts and solvates thereof.
20. A method of inhibiting DHFR *in vitro* comprising administering an effective amount of a compound selected from one or more of:
 - 15 (a) a compound of Formula I, as defined hereinabove;
 - (b) a compound of Formula II, as defined herein above;
 - (c) a compound selected from compounds 8-11 as shown in Table 1; and
 - (d) salts and solvates of (a), (b) and (c),
- 20 to a cell or assay mixture.
21. A use of a compound selected from one or more of:
 - (a) a compound of Formula I, as defined hereinabove;
 - (b) a compound of Formula II, as defined herein above;
 - 25 (c) a compound selected from compounds 8-11 as shown in Table 1; and
 - (d) salts and solvates of (a), (b) and (c),
- to inhibit DHFR *in vitro*.
- 30 22. The method according to claim 20, wherein the DHFR is bacterial DHFR.

-41 -

23. The method according to claim 22, wherein the bacteria are *E. coli*, *Bacillus Subtilis*, *Streptococci*, *Staphylococci*, *Enterococci*, *Salmonella*, *Haemophilus influenza*, *Pseudomonas aeruginosa*, *Bacillus anthracis* and *Helicobacter pylori*.

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24. The method according to claim 23, wherein the bacteria are *E. coli*.

25. The use according to claim 21, wherein the DHFR is bacterial DHFR.

10 26. The use according to claim 25, wherein the bacteria are *E. coli*, *Bacillus Subtilis*, *Streptococci*, *Staphylococci*, *Enterococci*, *Salmonella*, *Haemophilus influenza*, *Pseudomonas aeruginosa*, *Bacillus anthracis* and *Helicobacter pylori*.

15 27. The use according to claim 26, wherein the bacteria are *E. coli*.

28. The method according to any one of claims 20 and 23-24 wherein the compound is compound 9 as shown in table 1 and pharmaceutically acceptable salts and solvates thereof.

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29. The use according to any one of claims 21 and 25-27 wherein the compound is compound 9 as shown in table 1 and pharmaceutically acceptable salts and solvates thereof.

25 30. A method for identifying a candidate therapeutic agent and a cellular target molecule that is modulated by the agent comprising:

- (a) contacting a plurality of test agents with a first target cell;
- (b) selecting test agents from step (a) that inhibit the growth of the first target cell, wherein said selected test agents are candidate therapeutic agents;

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-42 -

- (c) contacting a candidate therapeutic agent identified in step (b) with (i) the first target cell and separately with (ii) a second target cell that overexpresses one or more genes;
- (d) comparing the growth of the first target cell with the second target cell
- 5 wherein the inhibition of growth of the first target cell and not the second target cell indicates that the second target cell overexpresses the cellular target molecule of the candidate therapeutic; and, optionally
- (e) isolating the cellular target molecule.

10 31. A method for identifying a candidate therapeutic agent and a cellular target molecule that is modulated by the agent comprising:

- (a) contacting a candidate therapeutic agent with (i) a first target cell and separately with (ii) a second target cell that overexpresses one or more genes;
- 15 (b) comparing the growth of the first target cell with the second target cell wherein the inhibition of growth of the first target cell and not the second target cell indicates that the second target cell overexpresses the cellular target molecule of the candidate therapeutic; and, optionally
- (c) isolating the cellular target molecule.

20 32. The method according to any one of claims 30-31 wherein the first and second target cells are selected from bacterial, fungus, parasites and cancer cells.

25 33. The method according to claim 32 wherein the bacterial cells are selected from the group consisting of *E. coli*, *Bacillus subtilis*, *Streptococci*, *Staphylococci*, *Enterococci*, *Salmonella*, *Haemophilus influenza*, *Pseudomonas aeruginosa*, *Bacillus anthracis* and *Helicobacter pylori*.

30 34. The method according to any one of claims 30-33 wherein the second target cell has been transformed with a multicopy random genomic library that overexpresses all of the genes present in the first target.

35. The method according to any one of claims 30-34, wherein the second target cell does not express genes encoding efflux pumps.

5 36. A pharmaceutical composition comprising a therapeutic agent identified using the screening method according to any one of claims 30-35 in admixture with a suitable diluent or carrier.

10 37. A method of preparing a pharmaceutical composition for use in therapy comprising mixing a therapeutic agent identified according to the screening assay according to any one of claims 30-35 with a suitable diluent or carrier.

15 38. A composition according to claim 36 or prepared using the method according to claim 37 wherein said therapeutic agent is for treating a bacterial infection, fungal infection, a parasitic infection or cancer.

20 39. A kit for use in identifying a therapeutic agent and its cellular target comprising a first target cell to which one wishes to generate a therapeutic agent and a second target cell that overexpresses one or more genes present in the first target cell.

40. A method of treating a disease comprising administering an effective amount of a therapeutic agent isolated according to the method of any one of claims 30 to 35 an animal in need thereof.

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41. A method of conducting a drug discovery business comprising:

(a) providing one or more assay systems for identifying a potential therapeutic agent based on the method according to any one of claims 30-35;

30 (b) conducting therapeutic profiling of agents identified in step (a), or further analogs thereof, for efficacy and toxicity in animals; and

-44 -

- (c) formulating a pharmaceutical preparation including one or more agents identified in step (b) as having an acceptable therapeutic profile.
- 42. A method of conducting a target discovery business comprising:
- 5 (a) providing one or more assay systems for identifying a potential therapeutic agent based on the method according to any one of claims 30-35;
- (b) (optionally) conducting therapeutic profiling of agents identified in step (a) for efficacy and toxicity in animals; and
- 10 (c) licensing, to a third party, the rights for further drug development and/or sales for agents identified in step (a), or analogs thereof.